

Mechanism of heart regeneration by cardiosphere-derived cells

Grant Award Details

Mechanism of heart regeneration by cardiosphere-derived cells

Grant Type: Basic Biology IV

Grant Number: RB4-06215

Project Objective: To investigate the mechanism of heart regeneration by cardiosphere-derived cells (CDCs) and test the hypothesis that CDCs promote regrowth of normal mammalian heart tissue through induction of adult cardiomyocyte cell cycle re-entry and proliferation.

Investigator:

Name:	Eduardo Marbán
Institution:	Cedars-Sinai Medical Center
Type:	PI

Disease Focus: Heart Disease

Human Stem Cell Use: Adult Stem Cell

Award Value: \$1,367,604

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 2

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Reporting Period: Year 3

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Grant Application Details

Application Title: Mechanism of heart regeneration by cardiosphere-derived cells

Public Abstract: In the process of a heart attack, clots form suddenly on top of cholesterol-laden plaques, blocking blood flow to heart muscle. As a result, living heart tissue dies and is replaced by scar. The larger the scar, the higher the chance of premature death and disability following the heart attack. While conventional treatments aim to limit the initial injury (by promptly opening the clogged artery) and to prevent further damage (using various drugs), regenerative therapy for heart attacks seeks to regrow healthy heart muscle and to dissolve scar. To date, cell therapy with CDCs is the only intervention which has been shown to be clinically effective in regenerating the injured human heart. However, the cellular origin of the newly-formed heart muscle and the mechanisms underlying its generation remain unknown. The present grant seeks to understand those basic mechanisms in detail, relying upon state-of-the-art scientific methods and preclinical disease models. Our work to date suggests that much of the benefit is due to an indirect effect of transplanted CDCs to stimulate the proliferation of surrounding host heart cells. This represents a major, previously-unrecognized mechanism of cardiac regeneration in response to cell therapy. The proposed project will open up novel mechanistic insights which will hopefully enable us to boost the efficacy of stem cell-based treatments by bolstering the regeneration of injured heart muscle.

Statement of Benefit to California: Coronary artery disease is the predominant cause of premature death and disability in California. Clots form suddenly on top of cholesterol-laden plaques in the wall of a coronary artery, blocking blood flow to the heart muscle. This leads to a "heart attack", in which living heart muscle dies and is replaced by scar. The larger the scar, the greater the chance of death and disability following the heart attack. While conventional treatments aim to limit the initial injury (by promptly opening the clogged artery) and to prevent further injury (using various drugs), regenerative therapy for heart attacks seeks to regrow healthy heart muscle and to dissolve scar. To date, cell therapy with CDCs is the only intervention that has been shown to be clinically effective in regenerating the injured human heart. However, the cellular origin of the newly-formed heart muscle and the mechanisms underlying its generation remain unknown. The present grant seeks to understand those basic mechanisms in detail, relying upon state-of-the-art scientific methods and preclinical disease models. The resulting insights will enable more rational development of novel therapeutic approaches, to the benefit of the public health of the citizens of California. Economic benefits may also accrue from licensing of new technology.

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